REMARKS

**Remark 1:**

Applicant notes that the Examiner claims O'Donnell teaches collagen "stimulation" and therefore is prior art to the present invention. Applicant submits, with all due respect, that is not correct. O'Donnell only teaches "photocoagulation" of collagen. Nowhere in the summary of the invention or the detailed description or claims does O'Donnell even use the word "stimulate" or "stimulation". The definitions of "coagulation" and "stimulation" are very different and have entirely different meanings.

First, according to Dorland's Medical Dictionary, "coagulation" is defined as: "the disruption of tissue by physical means to form an amorphous residuum, as in electrocoagulation and photocoagulation." In contrast, "stimulation" is defined as: "to excite functional activity in a part." As the Examiner can readily note, these are very different mechanisms and are taught differently in the patent literature. Coagulation is the destruction of tissue. Stimulation is the preservation and enhancement of tissue.

**Remark 2:**

The present invention teaches the use of much lower energies, shorter pulse lengths, and surface cooling specifically *to avoid coagulation* and to merely *stimulate* the production of collagen. Nowhere is the goal of coagulation of collagen indicated.

O'Donnell teaches much higher energies, longer pulse durations and visible, quantifiable tissue shrinkage that results from tissue coagulation. However, the present invention specifically teaches that there are no visible tissue changes after stimulation.

It has been discovered that coagulation and shrinkage of skin collagen does not work to reduce

wrinkles. In 1995, O'Donnell met with the Assignee of the present invention to discuss possible investment in Assignee's company. At that time, Assignee showed O'Donnell the work on collagen shrinkage and coagulation being performed since 1994. Assignee later abandoned those methods due to inefficacy. Assignee began clinical work using collagen stimulation instead, using non-coagulative energies levels as described in the present invention.

**Remark 3:**

The immediate shrinkage of collagen that is visible using the O'Donnell method is the result of collagen that has been completely destroyed. The body generates scar tissue and will slough off the coagulated "amorphous residue" with no long-term effect on wrinkles.

O'Donnell does not present experimental data or other evidence that the method he describes actually works. In fact, it has been shown that it does not work. Certain data related to extracted tissue histology doesn't account for the body sloughing off of the coagulated tissue. There has never been a successful product developed using O'Donnell's method. In comparison, however, there have been hundreds of studies by leading worldwide investigators and over 30 products now being sold that incorporate the "collagen stimulation" method described by Koop without coagulation.

An important difference or distinction between the present invention and cited prior art is the immediate post operative response of the treated skin. O'Donnell teaches that the skin should show immediate shrinkage and contraction of tissue.

The method of the present invention, in contrast, does not show immediate shrinkage or contraction. The immediate postoperative response is erythema, which is an indication that the body has been stimulated to generate new collagen.

**Remark 3:**

The use of growth factors enhances the "stimulation" of collagen even further. This process cannot work in conjunction with the O'Donnell method because the collagen is coagulated, i.e., dead and amorphic. O'Donnell does not describe the concept of "laser stimulation" taught by the present invention, and therefore the combination of a wound healing composition or growth factor is not obvious.

Coagulation only requires that collagen strands be heated to a minimum of about 70 degrees Celsius, such as taught by O'Donnell. He teaches the use of energies of at least 100 J/cm2 and at least 60 msec pulse length. This may be necessary to completely cook or coagulate the tissue to produce visible and immediate shrinkage.

Stimulation on the other hand as taught in the present invention requires much more careful selection of wavelength, energy, cooling and pulse duration to stimulate the response without coagulation and shrinkage. In particular only the wavelength region from 1320 to 1450 nm, about 30J/cm2, and 20-30 msec pulse duration with surface cooling actually works on patients. The present invention is a system for achieving "erythema and mild edema" without coagulation and shrinkage by carefully limiting the delivered energy.

The present invention teaches heating the papillary dermis to a " therapeutic level" to " initiate" a wound healing response. This wound healing response has been shown by many investigators to occur at energies that do not cause coagulation or shrinkage. From a clinical perspective, coagulation or shrinkage is a recognized clear sign of over treatment and is to be avoided to stimulate collagen production.

The use of a wound healing composition cannot work in conjunction with the teaching O'Donnell. Tt is not obvious based on a review of the cited prior art that an application of a wound

healing composition such as a growth factor would enhance collagen stimulation by laser energy as claimed in the present invention.

**Remark 4:**

In 6,106,514 O'Donnell teaches the use of anti inflammatories, anti oxidants and neo collagen promoters that are to be used post operatively to the laser treatment for 30 to 90 days. This is described in his patent in column 6 lines 46-50. He does not teach the mechanism of interaction of these drugs with the laser and makes no claims that the use of these drugs with the laser is any better than if they were used separately. Since he has grouped a broad range of well-known skin care pharmaceuticals together that all have different mechanisms of interaction he implies that there may not be any laser drug interaction benefit.

In contrast the present invention describes precisely how the wound healing compounds work to enhance collagen production. In particular, the present invention teaches that the drugs must be used in conjunction with a laser to be effective. There is a multiplying factor that makes the combination use more effective than the use of the laser or drug separately. Use of a drug post-operatively as taught by O'Donnell would not work as well and is not a claim of the present invention.

The key mechanism of action for the present invention is that the laser thermally injures the tissue causing the body to generate its own wound healing response. During the time that the body has been stimulated to generate new collagen, the drug application in conjunction with the laser will enhance this wound healing response that generates new collagen. This critical time has been shown to be within a few hours of laser application and while the skin exhibits erythema. The drug can also be administered immediately pre-operatively to prepare the body for the laser thermal injury and stimulation. Both the drug delivery and laser energy need to overlap or be in conjunction to be effective.

It is not obvious from prior art that the mechanism of laser stimulation of collagen and the mechanism of drug wound healing enhancement may be multiplied and enhanced when the two methods are used in conjunction. O'Donnell does not teach this.

**Remark 5:**

Hale does not teach a method which enhances the biological reaction in the skin, only that the drug is delivered to a site easier. Hale does not utilize electromagnetic energy to drive ions into the skin. He teaches the use of a static electric DC field only. An EM field is an alternating wave that radiates through free space with both positive and negative polarity swings. Radiowaves and lasers are examples of EM waves. EM waves do not drive ions across membranes, as suggested by Hale, but rather only cause ions to vibrate in place causing heat as is well known. In contrast, a static DC electric field as described by Hale may provide a force onto an ion and enable it to move across a membrane surface. Therefore, EM radiation cannot possibly work to deliver drugs using the teachings of Hale alone. Nowhere does Hale mention EM radiation such as microwaves or lasers in his invention. There is not even any mention of EM radiation anywhere, only DC electric fields.

Hale describes the use of direct current between two electrodes on the skin to generate about 1 milliamp of current into the skin, which transports the ionic drug along with it. This current can be generated with two wires hooked into a 9-volt battery. In contrast, an alternating electromagnetic wave as used in the present invention, such as a laser or microwave, requires a complex oscillator generator and an antenna or lens to allow the wave to propagate through space prior to hitting the skin. The mechanisms of the present invention and Hale are completely different. The method of the present invention is not obvious to one trained or skilled in the art, even in combination with Hale. The present invention does not claim enhanced penetration of the drug as Hale describes. The present invention is not claiming that the laser energy acts directly on the drug. Koop only claims that once the drug is present the

effect is enhanced by a thermal injury caused by the laser. Thus, one skilled in the art in the field could not use any teaching from Hale to anticipate the present invention.

**Remark 6:**

In the same manner, Purchio does not anticipate the present invention . Purchio teaches the use of chemotherapy and radiation treatment to increase the treatment efficiency. The radiation that Purchio describes is ionizing or particle radiation that has energy levels so high that tissue is destroyed on a molecular level and may become radioactive. This radiation is generated in a hospital synchrotron or from the nuclear decay of a radioactive particle such as Radium or Plutonium. This is a completely different mechanism with different equipment than is taught by the present invention. The present invention teaches the use of much lower energy electromagnetic waves in the visible or broadcast radio range that will only heat tissue, not disrupt it. Purchio does not describe the method of wound healing response. The goal of Purchio and his described radioactive treatment is to completely destroy tissue, not stimulate or enhance it. An expert in the field could not use any teaching from Purchio to anticipate the present invention.

Prior art that describes the use of a wound healing drug alone to enhance collagen production does not mention that the effect may be multiplied and enhanced by the application of laser energy to stimulate the body's wound healing response. The use of a laser in this way is not obvious to one skilled in the art.

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## CONCLUSION

Applicant respectfully submits that for all the foregoing reasons, the claimed subject matter describes patentable invention. Furthermore, Applicant submits that the specification is adequate and that the claims are now in a condition for allowance. No new matter has been entered.

Applicant hereby respectfully requests Examiner to withdraw the cited references as anticipating or obviating prior art, enter these amendments, find them descriptive of useful, novel and non-obvious subject matter, and authorize the issuance of a utility patent for the truly meritorious, deserving invention disclosed and claimed herein.

Without further, Applicant does not intend to waive any claims, arguments or defenses that they may have in response to any official or informal communication, paper, office action, or otherwise, and they expressly reserve the right to assert any traverse, additional grounds establishing specificity and clarity, enablement, novelty, uniqueness, non-obviousness, or other patentability, etc.

Further, nothing herein shall be construed as establishing the basis for any prosecution history or file wrapper estoppel, or similar in order to limit or bar any claim of infringement of the invention, either directly or under the Doctrine of Equivalents.

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Respectfully submitted,

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I hereby certify that this paper and the documents attached hereto are being deposited in a postage prepaid, sealed envelope with the United States Postal Service using First Class Mail service under 37 CFR 1.08 on the date indicated and is addressed to "Commissioner for Patents, Virginia 22313-1450". Signed: _____.
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